

Appl. No. : 09/076,404
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REMARKS

Following entry of the amendments submitted herewith, claims 19, 20, 26, 30, and 32-47 are pending. Claims 1-18, 21-25, 27-29, and 31 are canceled. Claims 19, 26, 32, and 34 are currently amended. Claims 36-47 are newly introduced.

As support for the claim amendments and additions is found throughout the specification as filed, no new matter is added by way of these amendments and additions.

For example, support for a "human target RNA," as recited in claims 19, 26, 32, and 34 is found at page 26, lines 29-31, which state that a target nucleic acid may belong to a higher organism such as a human. In claims 32 and 34, recitations of "RNA" or "target RNA" were replaced with "human target RNA," for consistency and clarity. The term "*in silico*" was inserted into the second recited step in claims 19, 26, 32, and 34 for clarity; support is found throughout the specification as filed, particularly at page 18, lines 14 to 17. Support for the additions to claim 26 is found in currently canceled claims 27-29, which depend from claim 26. Support for molecular interaction sites of less than 30 nucleotides, as recited in claims 36, 39, 42, and 45 is found at page 16, lines 1-2. Support for secondary structures recited in claims 37, 40, 43, and 46 is found at page 41, lines 12 to 14. Support for a secondary structure located within an untranslated region of a human target RNA, as recited in claims 38, 41, 44, and 47 is found throughout the specification as filed, in particular in Table 1, and on page 43, which describes methods for searching untranslated region databases for nucleic acids having secondary structures.

Discussion of Rejections Under 35 U.S.C. § 103(a)

Paragraph 9 of Office Action mailed April 17, 2006

Claims 19, 20, 26, 27, 29, 30, 32, and 33 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Murray et al. in view of Arenas et al. in view of Sezerman et al. in view of Greig et al. Applicants respectfully disagree. Claims 27 and 29 are canceled following entry of the amendments submitted herewith, rendering the rejection of these claims moot. Thus, the rejection will be addressed as it applies to claims 19, 20, 26, 30, 32, and 33.

The Examiner asserts that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the screening method of Murray et al., by use of

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the RNA targets of Arenas et al. because Arenas et al. show bioassays that screen for compounds that bind to RNA targets. The Examiner further contends that it would have been obvious to use mass spectrometry to analyze binding strength because Sezerman et al. shows that peptides may be analyzed *in silico* for binding, and Greig et al. shows that mass spectroscopy may be used to determine the binding affinity of a complex of a peptide and an oligonucleotide. Applicants respectfully submit that the Examiner has not met the burden required for a finding of a *prima facie* case of obviousness.

To establish a *prima facie* case of obviousness a three-prong test must be met. First, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success found in the prior art. Third, the prior art must reference must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). Furthermore, as affirmed by the Federal Circuit in *In re Kahn*, even though an invention may arise from a combination of elements, each of which is found in the prior art, “mere identification in the prior art of each element is insufficient to defeat the patentability of the combined subject matter as a whole.” The Court stated that a *prima facie* finding of obviousness based on a combination of elements in the prior art “must articulate the basis on which it concludes that it would have been obvious to make the claimed invention.” The Court further stated that this requires the explanation of “the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious.” See *In re Kahn*, 441 F.3d 977 (Fed. Cir. 2006), quoting *In re Rouffett*, 149 F.3d 1350 (Fed. Cir. 1998)

In providing only conclusory statements that the claimed invention is obvious, the Examiner has not met the burden required to establish a *prima facie* case of obviousness. In merely stating that it would have been obvious to modify the screening method of Murray with the teachings of Arenas, and that it would have been further obvious to use mass spectroscopy to analyze binding strength in view of the teachings of Sezerman et al. and Greig et al., the Examiner has not met the burden required to establish a *prima facie* case of obviousness. Moreover, the Examiner has not provided any explanation as to *why* one having ordinary skill in the art would have been motivated to modify the teachings of Murray et al. with those of Arenas et al., and further modify those teachings with the methods of Sezerman et al. and Greig et al.

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The Examiner has not provided any evidence, either in the references themselves or in the knowledge of one of ordinary skill in the art, for a motivation to combine the disparate methods described by the references in such a way as to render the claimed invention obvious. "A statement that modifications of the prior art to meet the claimed invention would have been 'well within the ordinary skill of the art at the time the claimed invention was made' because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a prima facie case of obviousness without some objective reason to combine the teachings of the references." *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). "To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references." *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985)

Federal Circuit decisions have consistently supported the notion that, in order for a claim to be held obvious in view of teachings of the prior art, a person of ordinary skill in the art must have some motivation to combine the teachings of the prior art in the particular manner claimed. See, for example, *In re Kotzab*, where the Court stated "Particular findings must be made as to the reason the skill artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed." *In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000) Additionally, as set forth in *In re Rouffet*, "[t]he examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed." *In re Rouffet*, 149 F.3d 1350 (Fed Cir. 1998) In *Teleflex v. KSR*, the Federal Circuit affirmed its earlier findings that the standard to be applied in the determination of obviousness requires "specific findings showing a teaching, suggestion, or motivation to combine prior art teachings in the particular manner claimed by the patent at issue." *Teleflex, Inc. v. KSR Int'l Co.*, 119 Fed. Appx. 282 (Fed. Cir. 2005) The arguments presented by the Examiner establish no motivation, either in the references themselves or in the knowledge of one skilled in the art, to combine the distinct teachings of Murray et al., Arenas et al., Sezerman et al., and Greig et al. to arrive at the claimed invention.

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Also required to establish a *prima facie* case of obviousness is that the references in combination teach or suggest each and every element of the claimed invention. The methods of Murray et al. and Sezerman et al. teach the *in silico* screening for compounds that bind to proteins. In contrast, the claimed methods identify *in silico* compounds that bind to human RNA targets. As is well known in the art, proteins and nucleic acids differ in both characteristics and behavior, and as such the methods taught by Murray et al. and Sezerman et al. are not applicable to methods of identifying *in silico* compounds that bind to a nucleic acid target. The additional teachings of Greig et al. and Arenas et al., which are directed to biochemical assays, not *in silico* methods, do not teach a means for modifying the methods of Murray et al. and Sezerman et al. in such a way as to make them applicable to nucleic acid targets, such as a human target RNA. Furthermore, the combination of references does not teach the identification of compounds that bind to a 'human target RNA.' As such, the combination of Murray et al., Arenas et al., Sezerman et al. and Greig et al. does not teach each and every limitation of the claimed method.

For these reasons, the Examiner's rejection fails to establish a *prima facie* case of obviousness, and Applicants respectfully request that the rejection of claims 19, 20, 26, 27, 29, 30, 32, and 33 be withdrawn.

Paragraph 8 of Office Action mailed April 17, 2006

Claims 21-23, 26-28, and 31 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Murray et al. in view of Arenas et al. in view of Vester et al. Applicants respectfully disagree. Claims 21-23, 27, 28, and 31 are canceled following entry of the amendments submitted herewith, rendering the rejections of these claims moot. Thus, the rejection will be addressed as it applies to claim 26.

The Examiner asserts that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the screening method of Murray et al., by use of the RNA targets of Arenas et al. because Arenas et al. show bioassays that screen for compounds that bind to RNA targets, and further obvious to use ribosomal targets because Vester et al. shows that ribosomal RNA is a site of action for antibiotics. Applicants respectfully submit that the Examiner has not met the burden required for a finding of a *prima facie* case of obviousness.

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As discussed above, to establish a *prima facie* case of obviousness a three-prong test must be met. First, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success found in the prior art. Third, the prior art must reference must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). Furthermore, there must be some explanation as to why “one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious.” See *In re Kahn*, 441 F.3d 977 (Fed. Cir. 2006), quoting *In re Rouffett*, 149 F.3d 1350 (Fed. Cir. 1998)

The Examiner asserts that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the screening method of Murray et al., by use of the RNA targets of Arenas et al. because Arenas et al. show bioassays that screen for compounds that bind to RNA targets, and to further modify using the teachings of Vester et al. for ribosomal RNA targets. As set forth in the foregoing remarks, the rejection establishes no teaching, suggestion or motivation that would encourage a person having ordinary skill in the art to combine the references to arrive at the claimed invention. Rather, the Examiner has made only conclusory remarks that the claimed invention is obvious in view of the cited references.

In addition to reciting the *in silico* generation and screening for compounds which bind to a human RNA target, pending claim 26 recites the steps of contacting the human target RNA with compounds identified in the *in silico* screen to provide a complex, ionizing the complex, fragmenting the complex, and determining whether the compounds bind to a molecular interaction site of the human target RNA. The Examiner relies upon Murray et al. for a screening method, Arenas et al. for RNA targets, and Vester et al. for ribosomal RNA targets. The combination of these three references does not teach each and every limitation of the method recited in claim 26. Furthermore, as discussed in the foregoing remarks, the combination of Murray et al., Arenas et al., Sezerman et al., and Greig et al., does not render obvious the method recited in claim 26.

For these reasons, the Examiner’s rejection does not establish a *prima facie* case of obviousness, and Applicants respectfully request that the rejection of claim 26 be withdrawn.

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Claims 35 and 35 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Murray et al. in view of Arenas et al. in view of Sezerman et al. in view of Greig et al., as set forth in paragraph 9 of the Office Action, and further in view of Nagai. Applicants respectfully disagree.

The Examiner asserts that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Murray et al. in view of Arenas et al. in view of Sezerman et al. in view of Greig et al. with the teachings of Nagai to arrive at methods of using an *in silico* virtual library of compound structure to identify a structure that binds snRNA, because Nagai shows that pre-mRNA, snRNA, and mRNA targets bind proteins and have important biological functions. Applicants respectfully submit that the Examiner has not met the burden required for a finding of a prima facie case of obviousness.

As discussed above, to establish a *prima facie* case of obviousness a three-prong test must be met. First, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success found in the prior art. Third, the prior art must reference must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). Furthermore, there must be some explanation as to why “one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious.” See *In re Kahn*, 441 F.3d 977 (Fed. Cir. 2006), quoting *In re Rouffett*, 149 F.3d 1350 (Fed. Cir. 1998)

As is the case for the 35 U.S.C. 103(a) rejection set forth in paragraphs 8 and 9 of the Office Action, the Examiner merely states that the claimed invention is obvious in view of the cited references, in this case in view of Murray et al., Arenas et al., Sezerman et al. and Greig et al. and further in view of Nagai, because Nagai teaches that pre-mRNA, snRNA and mRNA targets bind proteins and have important biological functions. It is well-established that a proper prima facie case of obviousness can only be put forth when there is found some objective reason to combine the teachings of the references. As set forth in the foregoing remarks, simply stating that the modifications would have been obvious to one of ordinary skill in the art because references that teach all aspects of the claimed invention that are individually known in the art is

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not sufficient to support a case of prima facie obviousness. Moreover, the rejection provides no evidence for a teaching, suggestion or motivation that would encourage a person having ordinary skill in the art to combine the references to arrive at the claimed invention.

For these reasons, the Examiner's rejection does not establish a *prima facie* case of obviousness, and Applicants respectfully request that the rejection of claims 34 and 35 be withdrawn.

Double Patenting

Applicants note that claims 19-23 and 26-35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-30 of copending application No. 10/104,949. Applicants will address this rejection upon indication of allowability of the present claims.

Conclusion

Applicants believe that all outstanding issues in this case have been resolved and that the present claims are in condition for allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is invited to contact the undersigned at the telephone number provided below in order to expedite the resolution of such issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 50-0252.

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